UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/652,791	08/29/2003	James McSwiggen	03-332-B (400.126)	3409

20306 7590 12/19/2005

MCDONNELL BOEHNEN HULBERT & BERGHOFF LLP
300 S. WACKER DRIVE
32ND FLOOR
CHICAGO, IL 60606

EXAMINER	
CHONG, KIMBERLY	

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 12/19/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/652,791	MCSWIGGEN ET AL.	
	Examiner	Art Unit	
	Kimberly Chong	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *36-69* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *36-69* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *29 August 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *12/1/03, 10/18/04*; 12/16/04
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's reply filed 06/30/2005 is acknowledged. The restriction requirement is moot due to Applicant's cancellation of said restricted claims.

Status of the Application

Claims 36-69 are pending in the application. Claims 1-35 are canceled. Claims 36-69 are currently under examination.

Priority

The claims of the instant application are accorded the priority date of 02/20/2003, the filing date of PCT/US03/05346. The instant application does not receive the benefit of the earlier filing date of the prior Provisional Applications because the claims are not supported by the specifications of the Provisional Applications and thus not supported by 35 U.S.C. § 112 first paragraph.

The Provisional Applications disclose short double stranded interfering nucleic acid (siNA) molecules targeted to various genes. However, the Provisional Applications do not disclose siNA targeted to a gene encoding ECGF1.

If Applicant believes the prior applications provide support then applicant must point, with particularity, to where such support can be found in the specification of the prior applications.

Therefore, the priority date granted to the instant claims is 02/20/2003.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 36-69 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-35 of copending Application No. 10/922,034. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims and the claims of the copending application are drawn to patently indistinguishable subject matter

The claims of the instant application is drawn to a double stranded short interfering nucleic acid (siNA) molecule, 18-27 nucleotides in length, targeted to ECGF1 wherein the siNA is chemically modified, each siRNA strand is complementary to the nucleotides of the other strand and the antisense or sense strands, the siNA comprises a cap structure, the siRNA antisense an sense strands are connected via a linker and the siNA is a pharmaceutically acceptable carrier or diluent.

Claims 1-35 of copending Application No. 10/922,034 are drawn to a double stranded short interfering nucleic acid (siNA), 18-23 nucleotides in length, targeted to ECGF1 wherein the siNA is chemically modified, each siRNA strand is complementary to the nucleotides of the other strand and the antisense or sense strands, the siNA comprises a cap structure, the siRNA antisense an sense strands are connected via a linker and the siNA is a pharmaceutically acceptable carrier or diluent.

Thus, claims 36-69 of the instant application overlap in scope with claims 1-35 of copending Application No. 10/922,034.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 48, 51-53, 56-60, 62 and 66 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 48 recites the limitation "wherein said sense region". There is insufficient antecedent basis for this limitation in the claim.

Claims 51, 53 and 56 recite the limitation "wherein pyrimidine nucleotides ". There is insufficient antecedent basis for this limitation in the claim.

Claims 52, 57-58 recite the limitation "wherein purine nucleotides ". There is insufficient antecedent basis for this limitation in the claim.

Claims 59-60 recites the limitation "wherein said sense region". There is insufficient antecedent basis for this limitation in the claim.

Claims 62 and 66 recites the limitation "wherein about 19 nucleotides". There is insufficient antecedent basis for this limitation in the claim.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 36-46 and 51-69 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wyatt et al. (U.S. Patent No: 6,716,975), Hammond et al. (Nature 2001), Tuschl et al. (WO 02/44321), Parrish et al. (Molecular Cell, 2000) and Cook et al. (U.S. Patent No. 5,587,471).

Claim 36 of the instant application is drawn to a double stranded short interfering nucleic acid (siNA) molecule comprising an antisense strand and a sense strand wherein each strand is 18 to 27 nucleotides in length and wherein the antisense strand if complementary to a nucleotide sequence of ECGF1 and the sense strand is complementary to the antisense strand. Claims 37-45 further limit claim 36 by reciting the siNA comprises chemically modified nucleotides, a phosphorothioate internucleotide linkage and wherein a non-nucleotide comprises an abasic moiety. Claims 46 and 51-69 further recite each siRNA strand comprises 19 to 23 nucleotides,

each strand comprises 19 nucleotides complementary to the nucleotides of the other strand and wherein the siNA comprises nucleotide or non-nucleotide linkers, comprises chemically modified nucleotides, a phosphorothioate internucleotide linkage and wherein a non-nucleotide comprises an abasic moiety, the 5' end optionally includes a 5'-phosphate and a pharmaceutical composition comprising the siNA and an acceptable carrier or diluent.

Wyatt et al. teach a nucleic acid molecule that is targeted to EDG1 (see column 3, lines 1-5 and Table 1) and comprises modified ribonucleotides or modified deoxyribonucleotides wherein the nucleic acid molecules are between 8-50 nucleotides in length and preferably 12-30 (see column 7, lines 35-58). Wyatt et al. further teach antisense compounds at least 19 nucleotides in length targeted to EDG1 (see Table 1) and further teach at least 8 consecutive nucleobases of the antisense compound are complementary to the target gene (see column 6, lines 9-40). Wyatt et al. further teach the nucleic acid molecule comprises chemically modified nucleotides at the 3' or 5' end (see column 10, lines 47-57). Wyatt et al. further teach phosphorothioate internucleotide linkages (see column 8, lines 58-63) and further comprise 2'-O-methyl (see column 10, lines 35-50) broadly comprise terminal cap moieties (see column 10, lines 50-68). Wyatt et al. do not teach a double-stranded nucleic acid molecule targeted to a EDG1 gene and further do not teach modified nucleotides comprising 2'-deoxy or 2'-deoxy-2'-fluoro.

Hammond et al. teach two methods for silencing specific genes: antisense and RNA interference. Hammond et al. teach that although antisense methods are straightforward techniques for probing gene function, the methods have suffered from "...questionable specificity and incomplete efficacy." (see page 110, column 1). Hammond et al. further teach

'...dsRNAs have been shown to inhibit gene expression in a sequence-specific manner" and further "RNAi is a potent method, requiring only a few molecules of dsRNA per cell to silence expression." Hammond et al. do not teach double-stranded nucleic acid comprising nucleotide comprising 2'-deoxy or 2'-deoxy-2'-fluoro, or comprising two separate strands connected via a linker molecule.

Tuschl et al. teach siRNA molecules which are 21 nucleotides in length and wherein each separate strand comprises at least 19 nucleotides complementary to the nucleotides of the other strand (Figure 14). Tuschl et al. further teach substitutions on either strand by 2'deoxy residues or 2'-O-methyl residues and further teach at least two 3' terminal nucleotides that are not base-paired to the nucleotides of the other strand (see Figure 14) and further teach 2'-deoxy thymidine, an abasic moiety, can be substituted for uridine at the 3' ends, i.e. a terminal cap. Tuschl et al. teach a 5'-phosphate on the antisense strand (see page 4, lines 12-20) and teach pharmaceutical compositions comprising double stranded nucleic acids and an acceptable carrier (see page 9, lines 17-25).

Parrish et al. teach a siRNA with an antisense or sense region comprising 2'-deoxy-2'-fluoro pyrimidine nucleotides (see Figure 5) and further teach this siRNA can mediate degradation of cellular RNA (see abstract page 1082).

Cook et al. teach oligonucleotides comprising glyceryl and various other conjugates and molecules that can be incorporated into oligonucleotides to increase the molecules pharmacokinetics.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to make a dsRNA targeted to a EDG1 gene, at taught by Wyatt et al. and further it

would have been obvious for one of ordinary skill in the art to make a dsRNA which are 21 nucleotides in length with chemical modifications, as taught by Tuschl et al., Parrish et al. and Cook et al.

One would have been motivated to use a dsRNA targeted to a EDG1 gene instead of an antisense because Hammond et al. teach using dsRNA to inhibit gene expression is more sequence specific than using antisense methodologies and RNAi using dsRNA is a more potent method requiring only a few molecules of dsRNA per cell and Tuschl et al. teach that siRNAs, compared with antisense or ribozyme, provide a new alternative to therapeutic methods of targeting genes. Further, Tuschl et al., Parrish et al. and Cook et al. provide motivation to incorporate chemical modifications into a dsRNA because the modifications are important for mediating RNA interference and important for the molecules stability.

Finally, one would have a reasonable expectation of success because Wyatt et al. teach antisense molecules can be targeted to a EDG1 gene and regulate gene expression, Hammond et al. teach that of the two methods used for silencing gene function, RNAi using dsRNA is more potent and sequence specific than antisense and finally Tuschl et al. and Parrish et al. teach making a dsRNA 21 nucleotides in length with chemical modifications is important for mediating RNAi and Cook et al. teach glyceryl can be incorporated to improve the oligonucleotides pharmacokinetics. Further, one would have a reasonable expectation of success because chemical modifications of an oligonucleotide adding stability and specificity to oligonucleotides were known in the art at the time of the invention was made. Additionally, one would expect such modifications would benefit siRNAs because such modifications had been shown to benefit antisense or ribozymes.

Thus in the absence of evidence to the contrary, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made.

Claims 36-44, 46-59 and 61-69 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wyatt et al. (U.S. Patent No: 6,716,975), Hammond et al. (Nature 2001), Tuschl et al. (WO 02/44321), Parrish et al. (Molecular Cell, 2000) and in further view of Matulic-Adamic (U.S. Patent No. 5,998,203) and Thomson et al. (Nucleic Acids Research 1993).

Claim 36 of the instant application is drawn to a double stranded short interfering nucleic acid (siNA) molecule comprising an antisense strand and a sense strand wherein each strand is 18 to 27 nucleotides in length and wherein the antisense strand if complementary to a nucleotide sequence of ECGF1 and the sense strand is complementary to the antisense strand. Claims 37-44 further limit claim 36 by reciting the siNA comprises chemically modified nucleotides, a phosphorothioate internucleotide linkage and wherein a non-nucleotide comprises an abasic moiety. Claims 46-59 and 61-69 further recite each siRNA strand comprises 19 to 23 nucleotides, each strand comprises 19 nucleotides complementary to the nucleotides of the other strand and wherein the siNA comprises nucleotide or non-nucleotide linkers, comprises chemically modified nucleotides, a phosphorothioate internucleotide linkage and wherein a non-nucleotide comprises an abasic moiety, the 5' end optionally includes a 5'-phosphate and a pharmaceutical composition comprising the siNA and an acceptable carrier or diluent.

Wyatt et al. teach a nucleic acid molecule that is targeted to EDG1 (see column 3, lines 1-5 and Table 1) and comprises modified ribonucleotides or modified deoxyribonucleotides wherein the nucleic acid molecules are between 8-50 nucleotides in length and preferably 12-30

(see column 7, lines 35-58). Wyatt et al. further teach antisense compounds at least 19 nucleotides in length targeted to EDG1 (see Table 1) and further teach at least 8 consecutive nucleobases of the antisense compound are complementary to the target gene (see column 6, lines 9-40). Wyatt et al. further teach the nucleic acid molecule comprises chemically modified nucleotides at the 3' or 5' end (see column 10, lines 47-57). Wyatt et al. further teach phosphorothioate internucleotide linkages (see column 8, lines 58-63) and further comprise 2'-O-methyl (see column 10, lines 35-50) broadly comprise terminal cap moieties (see column 10, lines 50-68). Wyatt et al. do not teach a double-stranded nucleic acid molecule targeted to a EDG1 gene and further do not teach modified nucleotides comprising 2'-deoxy or 2'-deoxy-2'-fluoro, or comprise two separate strands connected via a linker molecule.

Hammond et al. teach two methods for silencing specific genes: antisense and RNA interference. Hammond et al. teach that although antisense methods are straightforward techniques for probing gene function, the methods have suffered from "...questionable specificity and incomplete efficacy." (see page 110, column 1). Hammond et al. further teach " "...dsRNAs have been shown to inhibit gene expression in a sequence-specific manner" and further "RNAi is a potent method, requiring only a few molecules of dsRNA per cell to silence expression." Hammond et al. do not teach double-stranded nucleic acid comprising nucleotide comprising 2'-deoxy or 2'-deoxy-2'-fluoro, or comprising two separate strands connected via a linker molecule.

Tuschl et al. teach siRNA molecules which are 21 nucleotides in length and wherein each separate strand comprises at least 19 nucleotides complementary to the nucleotides of the other strand (Figure 14) and further teach 2'-deoxy thymidine, an abasic moiety, can be substituted for

uridine at the 3' ends, i.e. a terminal cap. Tuschl et al. further teach substitutions on either strand by 2'deoxy residues or 2'-O-methyl residues and further teach at least two 3' terminal nucleotides which are not base-paired to the nucleotides of the other strand (see Figure 14). Tuschl et al. teach a 5'-phosphate on the antisense strand (see page 4, lines 12-20) and teach pharmaceutical compositions comprising double stranded nucleic acids and an acceptable carrier (see page 9, lines 17-25).

Parrish et al. teach a siRNA with an antisense or sense region comprising 2'-deoxy-2'-fluoro pyrimidine nucleotides (see Figure 5) and further teach this siRNA can mediate degradation of cellular RNA (see abstract page 1082).

Matulic-Adamic et al. teach double stranded structures comprising abasic terminal cap moieties that provide resistance to degradation (see column 2, lines 44-55 and column 3 lines 1-68). Matulic-Adamic et al. further teach a double stranded structure comprising separate sense and antisense strands and further wherein this structure comprises a connecting loop comprising a linker or non-nucleotide linker (see Figure 3). Thomson et al. teach a similar structure to Matulic-Adamic wherein the double stranded structure comprising a linker (see Figure 1). Thomson et al. teach linkers increase efficiency of production and further enhance the molecules stability (see page 5602, second column).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to make a dsRNA targeted to a EDG1 gene, at taught by Wyatt et al. and further it would have been obvious for one of ordinary skill in the art to make a dsRNA which are 21 nucleotides in length with chemical modifications, as taught by Tuschl et al. and Parrish et al.

and further wherein the sense and antisense strands are connected via a linker, as taught by Matulic-Adamic et al. and Thomson et al.

One would have been motivated to use a dsRNA targeted to a EDG1 gene instead of an antisense because Hammond et al. teach using dsRNA to inhibit gene expression is more sequence specific than using antisense methodologies and RNAi using dsRNA is a more potent method requiring only a few molecules of dsRNA per cell. Further, Tuschl et al. and Parrish et al. provide motivation to make a dsRNA 21 nucleotides in length with chemical modifications because the length of the nucleotide and the modifications are important for mediating RNA interference and Matulic-Adamic et al. and Thomson et al. provide motivation to make a dsRNA with terminal cap moieties to provide resistance and degradation and further provide motivation to connect sense and antisense strands via a linker to increase efficiency of production.

Finally, one would have a reasonable expectation of success because Wyatt et al. teach antisense molecules can be targeted to a EDG1 gene and regulate gene expression, Hammond et al. teach that of the two methods used for silencing gene function, RNAi using dsRNA is more potent and sequence specific than antisense and finally Tuschl et al. and Parrish et al. teach making a dsRNA 21 nucleotides in length with chemical modifications is important for mediating RNAi and Matulic-Adamic et al. and Thomson teach the activity of the oligonucleotide comprising linkers do not have increase activity. Further, one would have a reasonable expectation of success because chemical modifications of an oligonucleotide adding stability and specificity to oligonucleotides were known in the art at the time of the invention was made. Additionally, one would expect such modifications would benefit siRNAs because such modifications had been shown to benefit antisense or ribozymes.

Thus in the absence of evidence to the contrary, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made.

Claims 36-46, 51-53 and 56-69 are rejected under 35 U.S.C. 103(a) as being unpatentable over Meacci et al. (Biochem 2002), Hammond et al. (Nature 2001), Tuschl et al. (WO 02/44321), Parrish et al. (Molecular Cell, 2000) and Cook et al. (U.S. Patent No. 5,587,471).

Claim 36 of the instant application is drawn to a double stranded short interfering nucleic acid (siNA) molecule comprising an antisense strand and a sense strand wherein each strand is 18 to 27 nucleotides in length and wherein the antisense strand if complementary to a nucleotide sequence of ECGF1 and the sense strand is complementary to the antisense strand. Claims 37-45 further limit claim 36 by reciting the siNA comprises chemically modified nucleotides, a phosphorothioate internucleotide linkage and wherein a non-nucleotide comprises an abasic moiety and a terminal cap. Claims 46, 51-53 and 56-69 further recite each siRNA strand comprises 19 to 23 nucleotides, each strand comprises 19 nucleotides complementary to the nucleotides of the other strand, comprises chemically modified nucleotides, a phosphorothioate internucleotide linkage and wherein a non-nucleotide comprises an abasic moiety, the 5' end optionally includes a 5'-phosphate and a pharmaceutical composition comprising the siNA and an acceptable carrier or diluent.

Meacci et al. teach a nucleic acid molecule targeted to EDG1 (see page 350) and comprises modified deoxyribonucleotides wherein the nucleic acid molecule is 21 nucleotides in length (see page 350). Meacci et al. do not teach a double-stranded nucleic acid molecule

targeted to a EDG1 gene and further do not teach modified nucleotides comprising 2'-deoxy or 2'-deoxy-2'-fluoro, or comprise two separate strands connected via a linker molecule.

Hammond et al. teach two methods for silencing specific genes: antisense and RNA interference. Hammond et al. teach that although antisense methods are straightforward techniques for probing gene function, the methods have suffered from "...questionable specificity and incomplete efficacy." (see page 110, column 1). Hammond et al. further teach " "...dsRNAs have been shown to inhibit gene expression in a sequence-specific manner" and further "RNAi is a potent method, requiring only a few molecules of dsRNA per cell to silence expression." Hammond et al. do not teach double-stranded nucleic acid comprising nucleotide comprising 2'-deoxy or 2'-deoxy-2'-fluoro, or comprising two separate strands connected via a linker molecule.

Tuschl et al. teach siRNA molecules which are 21 nucleotides in length and wherein each separate strand comprises at least 19 nucleotides complementary to the nucleotides of the other strand (Figure 14). Tuschl et al. further teach substitutions on either strand by 2'deoxy residues or 2'-O-methyl residues and further teach at least two 3' terminal nucleotides that are not base-paired to the nucleotides of the other strand (see Figure 14) and further teach 2'-deoxy thymidine, an abasic moiety, can be substituted for uridine at the 3' ends, i.e. a terminal cap. Tuschl et al. teach a 5'-phosphate on the antisense strand (see page 4, lines 12-20) and teach pharmaceutical compositions comprising double stranded nucleic acids and an acceptable carrier (see page 9, lines 17-25).

Parrish et al. teach a siRNA with an antisense or sense region comprising 2'-deoxy-2'-fluoro pyrimidine nucleotides (see Figure 5) and further teach this siRNA can mediate degradation of cellular RNA (see abstract page 1082).

Cook et al. teach oligonucleotides comprising glyceryl and various other conjugates and molecules that can be incorporated into oligonucleotides to increase the molecules pharmacokinetics.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to make a dsRNA targeted to a EDG1 gene, at taught by Meacci et al. and further it would have been obvious for one of ordinary skill in the art to make a dsRNA which are 21 nucleotides in length with chemical modifications, as taught by Tuschl et al., Parrish et al. and Cook et al.

One would have been motivated to use a dsRNA targeted to a EDG1 gene instead of an antisense because Hammond et al. teach using dsRNA to inhibit gene expression is more sequence specific than using antisense methodologies and RNAi using dsRNA is a more potent method requiring only a few molecules of dsRNA per cell and Tuschl et al. teach that siRNAs, compared with antisense or ribozyme, provide a new alternative to therapeutic methods of targeting genes. Further, Tuschl et al., Parrish et al. and Cook et al. provide motivation to incorporate chemical modifications into a dsRNA because the modifications are important for mediating RNA interference and important for the molecules stability.

Finally, one would have a reasonable expectation of success because Meacci et al. teach antisense molecules can be targeted to a EDG1 gene and regulate gene expression, Hammond et al. teach that of the two methods used for silencing gene function, RNAi using dsRNA is more

potent and sequence specific than antisense and finally Tuschl et al. and Parrish et al. teach making a dsRNA 21 nucleotides in length with chemical modifications is important for mediating RNAi and Cook et al. teach glyceryl can be incorporated to improve the oligonucleotides pharmacokinetics. Further, one would have a reasonable expectation of success because chemical modifications of an oligonucleotide adding stability and specificity to oligonucleotides were known in the art at the time of the invention was made. Additionally, one would expect such modifications would benefit siRNAs because such modifications had been shown to benefit antisense or ribozymes.

Thus in the absence of evidence to the contrary, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kimberly Chong whose telephone number is 571-272-3111. The examiner can normally be reached Monday thru Friday between 7-4 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached at 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public. For more information about the PAIR system, see http://pair-direct.uspto.gov.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Kimberly Chong
Examiner
Art Unit 1635